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EXAMINER	
DEJONG, ERIC S	

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1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,424	NAGALLA ET AL.	
	Examiner	Art Unit	
	ERIC S. DEJONG	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007 and 18 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-80 and 82-84* is/are rejected.

7)☒ Claim(s) *81* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicants response filed 07/02/2007 and 12/18/2007 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-84 are pending. Objected claim 81 has not been treated on its merits (see ***Claim Objections*** below). Claims 1-80 and 82-84 are currently under examination.

Specification

The objection to the abstract of the disclosure is with withdrawn in view of the amended abstract, filed 12/18/2007.

The objection to the disclosure for containing an embedded hyperlink and/or other form of browser-executable code is withdrawn in view of amendments made to the instant specification, filed 07/02/2007.

The objection to the specification for failing to provide proper antecedent basis for the claimed subject matter recited in claims 65, 67, 70, and 71 is withdrawn in view of amendments made to the instant claims, filed 07/02/2007.

The objection to the disclosure for fails to comply with Sequence Disclosure rules set forth the requirements of CFR § 1.821 through 1.825 is withdrawn in view of applicants submissions, filed 07/02/2007 and 12/18/2007.

Claim Objections

The objection to claims 1, 13, 29, 31, 40, 42, 52, 69, 70, 76, and 82 because of the minor informalities is withdrawn in view of amendments made to the instant claims, filed 07/02/2007.

The objection to claims 72-75 and 77-80 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only is withdrawn in view of amendments made to the instant claims, filed 07/02/2007. Further, claims 72-75 and 77-80 are now treated on the merits in the instant Office action.

Claim 81 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative only. See MPEP § 608.01(n). In the instant case, claim 81 depends from both claim 64 and 1. Accordingly, claim 81 not been further treated on the merits.

Response to Arguments

Applicant's arguments filed 07/02/2007 and 12/18/2007 have been fully considered but they are not persuasive.

In regard to the objection of claim 81 as being in improper form, applicants argue that the amendments made to the instant claim addresses this objection.

In response, it is noted that claim 81 was not altered in the amendment filed 07/02/2007 and remains dependent from both of the claims 1 and 64. Therefore, applicants argument is not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-80 and 82-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection of claims 1-71, 76, and 82-84 is maintained and reiterated from the previous Office action, mailed 01/03/2007.The rejection of claims 72-75 and 77-80 are necessitated by amendments made to the instant claims, filed 07/02/2007.

Claim 1 recites the limitation "the sequence in the sequence database" in lines 11 and 12 the instant claim. There is insufficient antecedent basis for this limitation in the instant claim. It is acknowledged that line 7 of claim 1 recites a plurality of

"sequences in a sequence database", however it remains unclear which of the plurality of sequences "the sequence" refers to. For the benefit of applicants, this rejection could be overcome by an amendment to the instant claim to recite "a sequence in the sequence database" in lines 11 and 12. Claims 2-80 are also included under this rejection due to their dependence from claim 1.

Claim 1 recites the limitation "the de novo sequence" in lines 12 and 17 of the instant claim. There is insufficient antecedent basis for this limitation in the instant claim. It is acknowledged that line 4 of claim 1 recites "producing at least one de novo sequence", however the antecedent basis for "the de novo sequence" remains unclear for embodiments where there is more than one de novo sequence. For the benefit of applicants, an amendment to the instant claim to recite "the at least one de novo sequence" would be sufficient to overcome the instant rejection. Claims 2-80 are also included under this rejection due to their dependence from claim 1.

Claim 82 recites the limitation "the sequence in the sequence database" in lines 10 and 11 the instant claim. There is insufficient antecedent basis for this limitation in the instant claim. It is acknowledged that line 7 of claim 82 recites a plurality of "sequences in a sequence database", however it remains unclear which of the plurality of sequences "the sequence" refers to. For the benefit of applicants, this rejection could be overcome by an amendment to the instant claim to recite "a sequence in the sequence database" in lines 11 and 12. Claims 83 and 84 are also included under this rejection due to their dependence from claim 82.

Claim 82 recites the limitation "the de novo sequence" in lines 11 and 16 of the instant claim. There is insufficient antecedent basis for this limitation in the instant claim. It is acknowledged that line 4 of claim 82 recites "producing at least one de novo sequence", however the antecedent basis for "the de novo sequence" remains unclear for embodiments where there is more than one de novo sequence. For the benefit of applicants, an amendment to the instant claim to recite "the at least one de novo sequence" would be sufficient to overcome the instant rejection. Claims 83 and 84 are also included under this rejection due to their dependence from claim 82.

Response to Arguments

Applicant's arguments filed 07/02/2007 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 112, second paragraph for indefiniteness, applicants argue that claims 1 and 82 have been amended to provide bases for the limitations "the sequence in the sequence database" and "the de novo sequence".

In response, it is acknowledged that applicants amendments to the instant claims have overcome the majority indefiniteness issues with the instant claims as identified in the previous Office action (see pages 6-13 of the previous Office action, mailed 01/03/2007). However, as set forth and reiterated in the above rejection, claims 1 and 82 still lack an antecedent basis for the recited limitations of "the sequence in the

sequence database" and "the de novo sequence". Therefore applicants arguments are not persuasive.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-80 and 82-84 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-80 and 82-82 are drawn to a drawn to a method for identifying sequences of molecules and sequence modification from mass spectrometry data. The claimed process comprises the abstract/computational steps of calculating at least one mass-based alignment, interpreting mass differences of modification sites, and calculating at least one match score, and, therefore, involves the application of a judicial exception. Regarding inventions involving the application of a judicial exception, said application must be a practical application of the judicial exception that includes either a step of a physical transformation, or produces a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the instant claims, there is no step of physical transformation that results from said application of judicial exception, thus the Examiner must determine if said application of a judicial exception produces a useful, concrete, and tangible result.

Claims 1-80 and 82-82 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. It is acknowledged that the independent claims have been amended to now recite a step of "storing said macromolecule list on a computer readable medium" (see for example, line 23 claim 1) and "storing said score on a computer readable medium" (see for example, line 17 of claim 82). However, these newly recited limitations are drawn to a result (either a macromolecule list or score) on a generic computer readable medium. The recited computer readable medium is further not limited to only physical computer readable media and as such encompasses the non-statutory embodiments of a carrier wave and signal. See *In re Nuitjen* (2007). Further, a result of storing a result in a computer readable medium does not serve to display or output any result to a user, or otherwise effectively communicate a result to a practitioner of the claimed invention. Therefore, the instant claim are not limited to producing only tangible embodiments, wherein a useful and concrete result of the method is displayed or output to a user, or otherwise effectively communicated to a practitioner of the claimed invention.

Response to Arguments

Applicant's arguments filed 07/02/2007 and 12/18/2007 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC 101 because the claimed invention is directed to non-statutory subject matter, applicants argue that the instant

claims have been amended to recite a step of storing a result on a computer readable medium, which is sufficient to overcome the instant rejection.

In response, it is reiterated from the instant rejection that the newly recited limitation is drawn to a storage of data in a computer readable medium. in a generic database. The recited "database is further not limited to only physical computer readable media, but further transient embodiments such as a carrier wave and signal. Further, the instant claims do not recite any other step of outputting or displaying a result to a user. Therefore, it is maintained that the instant claim are not limited to producing only tangible embodiments, wherein a useful and concrete result of the method is displayed or output to a user, or otherwise effectively communicated to a practitioner of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12, 63-80, and 82-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dancik et al. (J. Comp. Biol., 1999) in view of Pevzner et al. (see IDS filed 02/11/2005). The rejection of claims 1-12, 63-71, 76, and 82-84 are maintained and reiterated from the previous Office action mailed 01/03/2007. The rejection of claims 72-75 and 77-80 are necessitated by amendments made to the instant claims.

The instant claims are drawn to a method for identifying a macromolecule having a sequence and sequence modification thereof from mass spectrometry data comprising providing at least one de novo sequence from mass spectroscopy data, calculating at least one mass-based alignment between each de novo sequence and a sequence in a sequence database, comparing molecular masses of fragments to molecular masses of sequence fragments contained in a sequence database, interpreting mass differences of modification sites between sequences in said database and at least one de novo sequence using a modification catalog, and calculating at least one match score for the mass-based alignment. Further claimed embodiments of the method comprises the additional steps of identifying sequences in the sequence database from mass-based alignments in response to the match score, and grouping identification of sequences from at least one de novo sequence into an identified macromolecule list that agrees with the mass.

Dancik et al. sets forth a review of de novo peptide and protein sequencing techniques via tandem mass spectrometry and the development of a software algorithm, SHERENGA (see Dancik et al., Abstract). Dancik et al. further sets forth that SHERENGA addresses an art recognized need for the previously unsolved computation problems drawn to parameter learning, spectrum graphing, scoring schema, and sequencing algorithms (see Dancik et al., page 328, lines 24-45). Dancik et al. discloses methods for the identification of peptide and protein sequences using a tandem mass spectrometer capable of ionizing a mixture of peptides with different sequences and measuring their respective parent mass/charge ratios, selectively fragmenting each peptide into pieces and measuring the mass/charge ratios of the fragment ions (MS/MS spectra) and interpreting such MS/MS relies upon a data base searching (see Dancik et al., page 327, lines 1-11). Dancik et al. discloses that the automated SHERENGA further provides for improved *de novo* interpretation that automatically learns fragment ion types and intensity thresholds from a collection of test spectra generated from any type of mass spectrometer, wherein test data is used to construct optimal path scoring in the graph representations of MS/MS spectra and a ranked list of high scoring paths corresponding to potential sequences (see Dancik et al., Abstract and page 329, lines 1-27; page 330, lines 1 through page 333, line 9; and page 333, line 39 through page 336, line 5). Dancik et al. further disclose that peptides were obtained from in-gel or in-solution tryptic digestion of proteins isolated from yeast lysates, mouse plasma, and urine (see Dancik et al., page 338, lines 1-4). Dancik et al. further disclose an automated approach for scoring how well a candidate sequence "explains" a spectrum

and then and selecting sequences that provide a best fit to a given spectrum. The disclosed scoring method relies upon an evaluation of probability that a given sequence P produces a given spectrum S via maximizing a probability function p(P,S) (see Dancik et al., page 334, line 19 through page 336, line 5). Dancik et al. further provides results by the disclosed methods in Figures 5-9 (see Dancik et al. page 336, line 34 through page 337, line 20). Examples of interpretation with different quality are reflected by ambiguities in initial and/or terminal 1-3 amino acids (see page 336, line 34 through page 337, line 5). Dancik et al. further displays and labels mass objects relied upon to reflect different qualities of interpretation in Figure 10. To evaluate the performance of the disclosed de novo algorithms, Dancik et al. introduces the use of ladder difference metric between the predicted and actual sequences (see Dancik et al., page 337, lines 6-20).

While Dancik et al. sets forth the above discussed approaches to identifying sequences of molecules from mass spectrometry data, Dancik et al. does not fairly teach or suggest interpreting mass differences of modification between a sequence in a database and a de novo sequences that has been identified by mass based alignment as modifications in a modification catalog (see for example step (c) of instant claim 1).

Pevzner et al. sets forth methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry. Pevzner et al. further teach that the disclosed methods and algorithms address an art recognized need for algorithms that sort out reliable database hits from unreliable ones and identify mutated and modified peptides (see Pevzner et al., Abstract). Pevzner et al. further set

forth that the disclosed approaches demonstrate advantages over known prior art methods and further demonstrate the use of a spectral alignment approach as a filter in a new database search algorithm that reliably identifies peptides differing by up to two mutations/modifications from a peptide in a database (see Pevzner et al., Abstract). Figure 1 and Table 1 of Pevzner et al. list a plurality modified peptides used in the disclosed methods read on a modification catalog as instantly claimed. Further, Pevzner et al. rely upon MS/MS sequence methods to identify by mass based alignment to correlate sequence fragments to the modified peptides set forth in Figure 1 and Table 1 (see Pevzner et al., page 295, col. 2, line 43 through page 299, col. 1, line 15). Pevzner et al. further sets forth the application of spectral convolution of experimental and theoretical spectra that allow for the detection of mutations/modification without an exhaustive search (see Pevzner et al., page 292, col. 2, line 35 through page 294, col. 2, line 30). Figure 2 of Pevzner et al. further demonstrates the use of a set of differences matrixes, which are fairly interpreted as substitution matrixes, required to practice the spectral convolution procedures.

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use the disclosed methods for the identification of sequences using a tandem mass spectrometry, as set forth by Dancik et al., in combination with the methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry, as set forth by Pevzner et al. One of skill in the art would be motivated to combine the teachings of Dancik et al. and Pevzner et al. because Pevzner et al.

teaches that the disclosed methods and algorithms address an art recognized need for algorithms that sort out reliable database hits from unreliable ones and identify mutated and modified peptides. One of ordinary skill in the art would further recognize that the combination of Dancik et al. and Pevzner et al. would yield expected results.

Claims 1-27, 63-80, and 82-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dancik et al. in view of Pevzner et al., as applied to claims 1-12, 63-80, and 82-84 above, and further in view of Mann et al. (see IDS filed 02/11/2005). The rejection of claims 1-27, 63-71, 76, and 82-84 are maintained and reiterated from the previous Office action mailed 01/03/2007. The rejection of claims 72-75 and 77-80 are necessitated by amendments made to the instant claims.

The instant claims recite further embodiments comprising the steps of identifying a sequence in the sequence database with a tag match and generating a mass-based alignment between a de novo sequence and a sequence in the sequence database.

Dancik et al. in view Pevzner et al. provide for the above discussed methods of identifying sequences using a tandem mass spectrometry, as set forth by Dancik et al., in combination with the methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry, as set forth by Pevzner et al. However, neither Dancik et al. nor Pevzner et al. fairly teach or suggest identifying a sequence in a sequence database with a tag match (see for example, step (a) of instant claim 13).

Mann et al. demonstrate an approach to the identification of mass spectrometrically fragmented peptides (see Mann et al., Abstract). Mann et al. set forth that the disclosed methods as a means for interpreting complex tandem mass spectra by use of searching by peptide sequence tags (see Mann et al., page 4390, col. 2, lines 1-32). Mann et al. further demonstrate that MS/MS data can be relied upon for peptide identification with tags as short as two amino acids that can further be located in the presence of posttranscriptional modification or a sequence difference between the measured peptide and the peptide database (see especially Mann et al., page 4390, col. 2, lines 23-31 and page 4393, col. 1, line 25 through page 4397, col. 2, line 3).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use the disclosed methods for the identification of sequences using a tandem mass spectrometry, as set forth by Dancik et al., in combination with the methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry, as set forth by Pevzner et al., and in further combination with searching methods that rely on peptide sequence tags, as set forth by Mann et al. One of skill in the art would be motivated to combine the teachings of Dencik et al., Pevzner et al., and Mann et al., because Mann et al. teaches that the error tolerance of the peptide sequence tag approach is very high and is crucial in cases where predicted mass peptides is likely to be wrong (see especially, Mann et al., page 4398, col. 1, lines 22-37). One of ordinary skill in the art would further recognize that the combination of Dancik et al., Pevzner et al., and Mann et al. would yield expected results.

Claims 1-80, and 82-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dancik et al. in view of Pevzner et al. in view of Mann et al. as applied to claims 1-27, 63-71, 76, and 82-84 above, and further in view of Bader (Bioinformatics, 2003). The rejection of claims 1-71, 76, and 82-84 are maintained and reiterated from the previous Office action mailed 01/03/2007. The rejection of claims 72-75 and 77-80 are necessitated by amendments made to the instant claims.

The instant claims recite further embodiments comprising generating mass-based alignment using a breadth-first search (see for example instant claim 28).

Dancik et al. in view Pevzner et al. in view of Mann et al. provide for the above discussed methods of identifying sequences using a tandem mass spectrometry, as set forth by Dancik et al., in combination with the methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry, as set forth by Pevzner et al., and in further combination with searching methods that rely on peptide sequence tags, as set forth by Mann et al. However, neither Dancik et al., Pevzner et al., nor Mann et al. fairly teach or suggest generating mass-based alignment using a breadth-first search.

Bader sets forth methods related to extracting relevant complexes and pathways from high-throughput proteomics data sets to identify and extract networks are that essential to the art recognized problem of building pathways starting from known proteins of interest (see Bader, page 1869, col. 1, lines 1-10). Bader discloses the developed of an efficient algorithm, SEEDY, that extracts biologically relevant biological networks from protein–protein interaction data, building out from selected seed proteins.

The algorithm relies on a previous study establishing statistical confidence levels for interactions generated by two-hybrid screens and inferred from mass spectrometric identification of protein complexes (see Bader, page 1869, col. 1, lines 11-25). Bader further discloses the evaluation of the disclosed algorithm by use of a breadth-first outward search based on an outward traversal of a protein interaction network (see Bader, page 1870, col. 2, lines 5-22).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use the disclosed methods for the identification of sequences using a tandem mass spectrometry, as set forth by Dancik et al., in combination with the methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry, as set forth by Pevzner et al., in combination with searching methods that rely on peptide sequence tags, as set forth by Mann et al., and in further combination with the use of a breadth-first outward search based on an outward traversal of a protein interaction network, as set forth by Bader. One of skill in the art would be motivated to combine the teachings of Dencik et al., Pevzner et al., and Mann et al., because Bader teaches that the disclosed breadth-first outward search is applicable to the analysis of an algorithms inferred from mass spectrometric identification of protein complexes. One of ordinary skill in the art would further recognize that the combination of Dancik et al., Pevzner et al., Mann et al. and Bader et al. would yield expected results.

Response to Arguments

Applicant's arguments filed 07/02/2007 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Dancik et al. in view of Pevzner et al., applicants argue that the cited references when taken alone or in combination teach or suggest the identification of modifications using a modification catalogue as recited in the step (c) of instant claim 1.

In response, it is reiterated from the instant rejection that Pevzner et al. is relied upon for teaching methods drawn to efficient database searching for identification of mutated and modified proteins via mass spectrometry. Pevzner et al. further teaches the use of a spectral alignment approach as a filter in a new database search algorithm that reliably identifies peptides differing by up to two mutations/modifications from a peptide in a database. The listings of a plurality modified peptides used in the disclosed methods (see Figure 1 and Table 1 of Pevzner et al.) read on the use of a modification catalog to identify sequence modifications as instantly claimed. Neither the instant claims nor the instant specification provide a limiting definition for the contents of "a modification catalogue" that would exclude the listings of a plurality modified peptides as taught by Pevzner et al. Therefore applicants arguments are not found persuasive.

Applicants further argue that the method of Pevzner et al. for detecting mutations/modifications is not equivalent to interpreting mass differences and identifying the specific medications as disclosed in the instant specification.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., interpreting mass differences and identifying the specific medications) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claims do not recite any limitation that requires a specific modification be identified.

Applicants further argue that neither Dancik et al. nor Pevzner et al. teach methods for assembling identified peptides for the purpose of accurately identifying the macromolecule as recited in step (f) of claim 1 that requires grouping identifications of sequences into an identified macromolecule list.

In response, it is noted that claims 82-84 included under this rejection do not recite the additional process steps (f) as recited in claim 1. Further, Dancik et al. is relied upon in the instant rejection for teaching a scoring method that relies upon an evaluation of probability (see Dancik et al., page 334, line 19 through page 336, line 5) and disclosing a listing grouped of identified sequences resulting from the disclosed mass based alignment methodology (see Figures 8 and 9 of Dancik et al.), which reads on grouping identifications of sequences into an identified macromolecule list as instantly claimed.

In regards to the rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Dancik et al. in view of Pevzner et al., and further in view of Mann et al., applicants argue that Mann et al. does not disclose each and every limitation of claim 1, therefore the instant claims are not anticipated by Mann et al.

In response, it is noted that the instant claims are rejected under 35 USC § 103(a) and not 35 USC § 102(b). Therefore applicants argument that the instant claims are not anticipated by Mann et al. is not germane to the basis of the instant rejection.

Applicants further argue the instant claims are not obvious over Dancik et al. in view of Pevzner et al. in view of Mann et al. because Mann et al. does not seek to locate or identify modification sites, but rather teaches away from this step in stating "[i]t may however, only be possible to locate the modification within several amino acids if the required fragment ions are missing from the tandem mass spectrometer" on page 4397, col. 2, paragraph 1.

In response, it is noted that the instant claims do not recite a limitation drawn "locating or identifying a modification site". Therefore, applicants argument that the prior art of Mann et al. teaches away from the claimed invention is not persuasive.

In the instant rejection, Mann et al. is relied upon for teaching an approach to the identification of mass spectrometrically fragmented peptides and means for interpreting complex tandem mass spectra by use of searching by peptide sequence tags (see Mann et al., Abstract and page 4390, col. 2, lines 1-32).

In regards to the rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Dancik et al. in view of Pevzner et al. in view of Mann et al. in view of Bader, applicants argue that the relevance of Bader is unclear and that the disclosed methods therein are unrelated to the instant application.

In response to applicant's argument that Bader is nonanalogous (unrelated) art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, it is reiterated from the instant rejection that the breadth-first outward search is taught by Bader teaches as being applicable to the analysis of an algorithms inferred from mass spectrometric identification of protein complexes. Therefore, the prior art reference of Bader is in the field of applicant's endeavor drawn to methods for identifying a macromolecule having a sequence and sequence modification thereof from mass spectrometry data.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Moran Marjorie can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric S DeJong
Primary Examiner
Art Unit 1631

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